

AMENDMENTS TO THE CLAIMS

1. (Previously presented) A polyclonal, monoclonal, chimeric, humanized, human or anti-anti-idiotype antibody or fragment thereof being capable of specifically binding the amino acid sequence set forth in SEQ ID NO: 5, SEQ ID NO: 6, and/or SEQ ID NO: 3, wherein the amino acid sequence comprises a phosphorylated threonine at amino acid position 559 of SEQ ID NO: 5, position 26 of SEQ ID NO: 6, or position 11 of SEQ ID NO: 3, and wherein the antibody or fragment thereof does not bind the non-phosphorylated amino acid sequence set forth in SEQ ID NO: 5, SEQ ID NO: 6, or SEQ ID NO: 3.
2. (Currently amended) The antibody or fragment thereof according to claim 1, wherein the amino acid sequence is the amino acid sequence of SEQ ID NO: 5 ~~SEQ ID NO: 6~~.
3. (Canceled)
4. (Previously presented) The antibody or fragment thereof of claim 1, wherein said antibody is an IgG antibody.
5. (Previously presented) The antibody or fragment thereof of claim 1, wherein said antibody fragment is selected from the group consisting of a single-chain Fv, an Fab, an Fab', and an F(ab')₂.
6. (Previously presented) The antibody or fragment thereof of claim 1, wherein said antibody or antibody fragment is further capable of regulating a biochemical activity of a NIK molecule.
7. (Previously presented) The antibody or fragment thereof according to claim 1, wherein said antibody or fragment thereof is further capable of specifically detecting phosphorylated NIK or a specific portion thereof.
8. (Previously presented) The antibody or fragment thereof according to claim 7, wherein said antibody or fragment thereof is capable of specifically detecting phosphorylated NIK by Western immunoblotting analysis.

9. (Previously presented) The antibody or fragment thereof according to claim 7, wherein said antibody or fragment thereof is capable of specifically detecting phosphorylated NIK by ELISA.

10. (Previously presented) The antibody or fragment thereof according to claim 7, wherein said antibody or fragment thereof is capable of specifically detecting phosphorylated NIK by immunoprecipitation.

11. (Previously presented) The antibody or fragment thereof according to claim 1, wherein the antibody is a monoclonal antibody generated by hybridoma NIK-P4 30.12 deposited at the Collection Nationale de Culture de Microorganismes (CNCM) under No. I-3095.

12. (Currently amended) A polyclonal, monoclonal, chimeric, humanized, human or anti-anti- idiotype antibody or fragment thereof being capable of specifically binding NIK comprising a phosphorylated threonine at amino acid position 559 of SEQ ID NO: 5, the antibody prepared by immunizing a mammal with the amino acid sequence set forth in ~~SEQ ID NO: 5~~, SEQ ID NO: 3 and/or SEQ ID NO: 6, wherein the amino acid sequence comprises a phosphorylated threonine at amino acid ~~position 559 of SEQ ID NO: 5~~, position 26 of SEQ ID NO: 6, or position 11 of SEQ ID NO: 3.

13. (Previously presented - Allowed) A hybridoma clone deposited at the Collection Nationale de Culture de Microorganismes (CNCM) under No. I-3095

14. (Previously presented) A pharmaceutical composition comprising a pharmaceutically acceptable carrier and, as an active ingredient, a polyclonal, monoclonal, chimeric, humanized, human or anti-anti-idiotype antibody or fragment thereof being capable of specifically binding the amino acid sequence set forth in SEQ ID NO: 5, SEQ ID NO: 6, and/or SEQ ID NO: 3, wherein the amino acid sequence comprises a phosphorylated threonine at amino acid position 559 of SEQ ID NO: 5, position 26 of SEQ ID NO: 6, or position 11 of SEQ ID NO: 3.

15. (Previously presented) The pharmaceutical composition according to claim 14, wherein the amino acid sequence is the amino acid sequence set forth in SEQ ID NO: 3.

16. (Original) The pharmaceutical composition according to claim 14, wherein said antibody is an IgG antibody.

17. (Previously presented) The pharmaceutical composition according to claim 14, wherein said antibody or antibody fragment is a polyclonal, monoclonal, chimeric, humanized, or anti-anti-idiotype antibody or fragment thereof from murine origin.

18. (Previously presented) The pharmaceutical composition according to claim 14, wherein said antibody fragment is selected from the group consisting of a single- chain Fv, an Fab, an Fab', and an F(ab')₂.

19. (Previously presented) The pharmaceutical composition according to claim 14, wherein said antibody or fragment thereof is further capable of regulating a biochemical activity of a NIK molecule.

20-25. (Cancelled)

26. (Withdrawn) A method of regulating a biochemical activity of a NIK molecule, the method comprising contacting the NIK molecule with a polyclonal, monoclonal, chimeric, humanized, human or anti-anti-idiotype antibody or a fragment thereof being capable of specifically binding the amino acid sequence set forth in SEQ ID NO: 5, or a portion thereof wherein the amino acid sequence or portion thereof comprises a phosphorylated threonine at amino acid position 559 of SEQ ID NO: 5, thereby regulating a biochemical activity of a NIK molecule.

27. (Withdrawn) The method according to claim 26, wherein said contacting the NIK molecule with said antibody is effected by administering said antibody to an individual.

28. (Withdrawn) The method according to claim 26, wherein said antibody is an IgG antibody.

29. (Withdrawn) The method according to claim 26, wherein said antibody or antibody fragment is of murine origin.

30. (Withdrawn) The method according to claim 26, wherein said antibody fragment is selected from the group consisting of a single-chain Fv, an Fab, an Fab', an F (ab')2 and a CDR.

31. (Withdrawn) A composition-of-matter comprising a substrate covalently attached to a peptide of amino acid sequence set forth in SEQ ID NO: 5, or a portion thereof wherein the amino acid sequence or portion thereof comprises a phosphorylated threonine at amino acid position 559 of SEQ ID NO: 5 for selectively capturing the antibody or antibody fragment capable of specifically binding the target antigen.

32. (Withdrawn) The composition-of-matter according to claim 31, wherein the portion thereof comprises the amino acid sequence set forth in SEQ ID NO: 3.

33. (Withdrawn) The composition-of-matter of claim 31, wherein said substrate is an affinity chromatography matrix.

34. (Withdrawn) The composition-of-matter according to claim 31, wherein said substrate comprises a carbohydrate or a derivative of said carbohydrate.

35. (Withdrawn) The composition-of-matter according to claim 31, wherein said carbohydrate is selected from the group consisting of agarose, sepharose, and cellulose.

36. (Withdrawn) The composition-of-matter according to claim 31, wherein said substrate is selected from the group consisting of a bead, a resin, or a plastic surface.

37-44. (Cancelled)

45. (Withdrawn) A method for preparing a monoclonal antibody comprising growing a cloned hybridoma comprising a spleen cell from a mammal immunized with an amino acid sequence comprising SEQ ID NO: 6, or a portion thereof wherein the amino acid sequence or portion thereof comprises a phosphorylated threonine at amino acid position 559 of SEQ ID NO: 5 and a homogeneic or heterogeneic lymphoid cell in liquid medium or mammalian abdomen to allow the hybridoma to produce and accumulate the monoclonal antibody.

46. (Withdrawn) A method according to claim 45, wherein the portion thereof comprises amino acid sequence set forth in SEQ ID NO: 3.

47. (Withdrawn) A method for identifying a ligand capable of inducing NIK-mediated NFKB activation in a cell, comprising introducing an antibody or an antibody fragment according to anyone of claims 1 to 12 into a cell, incubating the cell with individual ligands, monitoring parameters indicative of NFKB activation, and selecting the ligand by which activation of NFKB is affected by specific blockage of NIK activity by said antibody or antibody fragment.

48. (Withdrawn) A method according to claim 47, wherein activation of NFKB is determined by monitoring parameters indicative of the canonical pathway activation of NFKB.

49. (Withdrawn) A method according to claim 48, wherein activation of NFKB is determined by monitoring IxB_a degradation.

50. (Withdrawn) A method according to claim 49, wherein the cells are of lymphoblastoid type.

51. (Withdrawn) A method according to claim 50, wherein the cells are selected from Ramos, BJAB, and Jurkat cells.

52. (Withdrawn) A method of treatment of a disease caused or aggravated by the activity of NIK, comprises the administration of a polyclonal, monoclonal, chimeric, humanized, human or anti-anti-idiotype antibody or fragments thereof being capable of specifically binding the amino acid sequence set forth in SEQ ID NO: 5, or a portion thereof wherein the amino acid sequence or portion thereof comprises a phosphorylated threonine at amino acid position 559 of SEQ ID NO: 5 to an individual in need.

53. (Withdrawn) The method according to claim 52, wherein said antibody is an IgG antibody.

54. (Withdrawn) The method according to claim 52, wherein said antibody or antibody fragment is derived from mouse.

55. (Withdrawn) The method according to claim 52, wherein said antibody fragment is selected from the group consisting of a single-chain Fv, an Fab, an Fab', an F (ab') 2 and a CDR.

56. (Withdrawn) The method according to claim 52, wherein the disease is selected from a malignant diseases and diseases associated with pathological immune responses.

57. (Withdrawn) The method according to claim 56, wherein the disease associated with pathological immune responses is selected from autoimmune, allergic, inflammatory, and transplantation-related diseases.

58. (Withdrawn) The method according to claim 57, wherein the disease is selected from, asthma, rheumatoid arthritis, inflammatory bowel disease, atherosclerosis and Alzheimer's disease.

59. (Withdrawn) The method according to claim 56, wherein the disease is a malignant disease.

60. (Withdrawn) A method for the purification of a NIK binding protein, which comprises contacting a sample containing NIK and the NIK-binding protein with an antibody according to claim 1, co-immunoprecipitating the NIK and NIK-binding protein, washing the immune complex produced, and recovering the NIK-binding protein from the immune complex using a competing peptide derived from NIK.

61. (Withdrawn) The method according to claim 60, wherein the sample is selected from body fluids, cell extracts and DNA expression libraries.

62-63. (Cancelled)